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Modus Operandi of Medicines
W. C. Brewster

Paſsed March 9th
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W. E. H
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A
Summary Diſsertation
On The
Modus Operandi
of
MEDICINES

Submitted to the
MEDICAL FACULTY
For The Degree
OF
DOCTOR OF MEDICINE
BY
William Carll Brewster
of
PENNSYLVANIA

To

N. Chapman, M.D.

Respected Sir,

Difficult operations require able hands. So universal is the application of this remark, that it will hold good in every department of science and mechanics. No one for instance will commence an undertaking, to accomplish which great exertion is neceſsary, unleſs he is conscious that he poſseſses a sufficient degree of muscular power. So in science, the solution of abstruse questions is or ought to be committed to competent persons.

If this be true, and the accumulated experience of ages proves it so, what apology shall I offer for engaging in a subject, which notwithstanding all that has been said, is still undeniably wrapt in the most profound and mysterious obscurity; - a subject on which the sun of science has scarcely shed a single beam of light; and a subject which has baffled all the attempts and defeated all the endeavours of the most able, expert and ingenious physiologists to unravel its intricacies. Confessedly, Sir, the Modus Operandi of Medicines is obscure, and requires for its explanation talents of a superior cast. And although my unaspiring genius would not dare advance a single opinion of its own on the subject, yet I trust I may say without danger of incurring the imputation of pedantry, that I can compile the various sentiments which different authors hold, (and

the arguments by which these sentiments are attempted to be sustained. This is accordingly my object. — But it is not for a Candidate humble as I am, to come forward at this early stage of the case, before a member of that faculty on the iſsue of whose decision my destiny for life depends, and ostentatiously state the manner in which that object is herein accomplishd. This rests alone with you. — And if upon a candid and impartial examination, you shall consider my compendium worthy of notice, I feel confident that you will give it all that credit to which its merits entitle it. For myself, conscious as I am of my imperfections, I depend entirely on your indulgence.

I am, dear Sir, very respectfully,
Your obedient servant,
William Carll Brewster

To explain the operation of medicines two doctrines at present prevail:

1st Medicines are absorbed into the circulation, and produce their effect by means of the blood.

2nd Medicines operate alone on the solids, their impression being extended through the medium of Sympathy. Against the first of these hypotheses I most candidly confess that I have a personal prejudice. This circumstance however shall not in the least prevent me from going over all the grounds on which its partizans rest their dependance for the establishment of their doctrine

In the dark ages of ignorance and delusion, when nought was

known but a sacred veneration for old opinions, and a blind devotion to magisterial authority, science lay almost dormant. We are therefore not to be surpris'd to hear of the prevalence of many strange and gratuitous notions. Among these the blood was suppos'd to undergo changes in quantity, consistence, temperature &c. Hence the origin of the terms Inspiſsants, Attenuants, Diluents, Refrigerants &c. Opinions, however, so totally groundleſs were destined to have but a temporary continuance. The increase of knowledge soon exposed their fallacy, and accordingly they were abandoned by all discerning, scientific philosophers. Notwithstanding this however, there are still those who profeſs to believe that certain medicines are absorbed into the circulation. Such an opinion appears to me altogether inconsistent with the nature of the blood; and I do

maintain that it never has, and never can be proved by any direct or positive evidence.

Every substance that is taken into the stomach, whether aliment or medicine is alike exposed to the powers of digestion. By this process all the original compounds are decomposed, and one complete homogeneous mass is formed. Now it is evident that no medicines can reach the seat of absorption in their nascent state, and of course cannot be absorbed as medicines. This would seem to strike the doctrine at the very root. To get over the insurmountable difficulty, we must either suppose that there are Lacteals in the stomach, or that the gastric juice has no power of operating upon medicines; the very converse of both of which is known to be the case.

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Moreover the Lactiferous absorbents display a species of elective attraction, amounting almost to fastidiousneſs; carefully selecting every thing that is nutritious, and uniformly rejecting every thing that might in any way prove detrimental. And how can it be supposed that they should admit a substance into the circulation which experiment proves to produce almost certain death when introduced artificially? The thing in itself is next to preposterous; and these two circumstances alone which I have mentioned would seem to forbid the poſsibility of medicinal absorption.

But these are not the only grounds on which the doctrine may be combatted. Supposing that the Lacteals

were incapable of rejecting what is injurious;— the substance absorbed would penetrate to the first conglobate gland, which would take on inflammation, and arrest its further progress. This we know perfectly well to be the case: and a good exemplification of the position we have in the production of Bubo from the absorption of the Syphilitic virus.

But admitting that medicines do enter the circulation, the whole mass of blood in this case must be equally charged with the substances, and of course while a salutary action is going on in a diseased organ, every other part of the system must suffer. This could not fail to be the case. When a bowl of soup is placed on the table, if it is seasoned very high with pepper, salt, nutmeg &c, the substance thus medicated may suit one palate, while

perhaps it may disagree with all the rest of the company. This example, coarse as it is, serves very well to illustrate my meaning. The reasonableness of the supposition must be obvious to every impartial observer. Why shall a medicine after it has arrived in the blood be determined to any one part in preference to another; (and why shall it not produce its peculiar effect on every organ in the whole system? To this very natural interrogatory a satisfactory answer never has been given.

Moreover we know perfectly well that the effects of certain articles are perceived in a much shorter time than they would be, provided they were absorbed into the circulation. Examples of this fact we have in the almost instantaneous stimulus of ardent spirits, in the soporific effects of

Opium, (and the anti-febrile qualities of Cinchona.

Again, if medicines entered the blood, it is very reasonable to suppose that they should be found in that fluid. This however, does not appear to be the case. In an experiment, Dr. Wollaston gave a person a quantity of Pruſsiate of Potash: but after a lapse of four hours, upon an examination of the blood, no Pruſsiate was to be found in its Serum. — In opposition to this however, we are told by Mr. Brande, one of most eminent chemists in Europe, that he administered Soda to a patient for a long time, and in a large quantity, and then (mirabile dictu!) he detected the substance in the blood; which he might have done, had his patient never seen a particle of Soda, much leſs taken it. It is perfectly well known that in a

natural state Soda is one of the constituents of blood: (and I am astonished to find that so great a man should undertake to support a favourite doctrine on such flimsy evidence as this.

In addition to all this it may be stated that extraneous substances of any kind when injected into the circulation produce very serious consequences. The most bland articles, as milk, chyle &c. have been known to occasion distressing effects; and Bichat states that in several cases even a bubble of air caused immediate death. Innumerable experiments have been made on the subject with precisely similar results; so that this point appears to be pretty well settled. And besides, the most zealous upholders of the opposite doctrine do not hesitate to admit the

truth of the fact, though they attribute it to a very frivolous circumstance. The fact is medicines are extraneous substances, and as such they have no busineſs to circulate throughout the system with a vital fluid like the blood.

With such an overwhelming maſs of evidence as this, what unconfiding sceptic can doubt of the Operation of Medicines being entirely independent of the Circulation? If such an one there is, let him have his doubts removed by the known fact that many substances produce their full effect though the heart and blood-veſsels be taken away: so that in this case they could not poſsibly enter the circulation. Experiments, the relation of which I am merely transcribing from a known source, and to which I may incidentally remark I am indebted for many of the ideas

The lines erased in pages 13 & 14, were denied by the Candidate, as intending any thing personal to one of the Professors, who objected to the retaining the paragraphs in the Thesis – It was immediately agreed to by the Candidate that it should be erased.

J R Coxe. – March 8th 1824

I have advanced in this treatise, experiments I say, made by Whytt and Girtanner; (and repeated by other equally respectable experimentalists, sufficiently confirm the truth of the fact above stated.

~~Notwithstanding all this however, there are still those who profess to believe that medicines enter the circulation and produce their effects in this way: and the profession I am warranted in saying is all. For I cannot think that in these enlightened days there are any who really believe the doctrine they endeavour to support. If they did, why do they not in some cases of Dysphagia and Tetanus propose the injection of medicines into the veins? This is a very natural interrogatory; and until it is answered, I am fully warranted in~~

~~saying that they do not in fact believe their own doctrine. It is more therefore from a desire of maintaining extravagant and favourite opinions than of benefiting science, that these eccentric partizans labour to confirm sentiments which are totally incompatible and altogether inconsistent with the known laws of the human system. But without pursuing this disagreeable enquiry any further, I shall proceed to examine the weak grounds on which the doctrine is attempted to be established.~~

Prior to this however, I may remark what I have heretofore done, that medicines have never been detected in the circulation. The careful, well-conducted, and very candid experiment, to which I formerly alluded, made by Dr. Wollaston, leaves no doubt on this subject. Similar results have

invariably followed all subsequents attempts. In fact the most strenuous upholders of the doctrine do not pretend that they have ever traced medicines further than the Thoracic Duct, or at most, the Mesenteric veſsels. And when we recollect that these experiments were made by men blinded by preconceived notions and determined at all events to support a favourite opinion, I think we need offer no apology for strongly doubting their validity. As for myself, casting forth as I do from the humble receſses of obscurity a dim glance on the all-resplendent Sun of science, I should not at all hesitate in pronouncing these statements wilful exaggerations, or in discediting their authenticity altogether. The men who performed these experiments, however respectable, it must be remembered had their own opinions to support. Situated in such circumstances, they could

only see through the glaſs of bias: and what was deficient in reality, their own fertile imaginations were ever ready to supply.

Discarding then as I do all evidence of direct experiment, I shall proceed to examine some acceſsory circumstances which it is supposed favour the supposition of Medicinal Absorption.

It is well known that after eating strong-smelling articles, such as Garlic, Onions &c. the peculiar odour of these substances is perceived in the breath: hence it is inferred that they must have entered the blood. Such a conclusion however, is entirely unwarrantable. Every one must know that the substance might give out its odour in the stomach as well as in the open air: and that this odour might spread

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by exhalation, or rise by specific levity up through the Oesophagus, and mingling with the breath, its properties might thus become perceptible to the sense of smell. This explanation is not at all forced. Analogy supports it. Thus in cases of ulcerations of the Tonsils or Fauces, or in case of a carious tooth, a disagreeable smell is evident in the breath. Now this fact is altogether independent of the Lungs. Besides the before-mentioned effects take place in a much shorter space of time than would have been occupied by the passage of the substances in question through the rout of the circulation. But what puts this matter beyond all reach of controversy, and completely establishes the explanation I have ventured to suggest, is that the odour of the above articles is perceived although the act of respiration be entirely suspended. This experiment I have tried

repeatedly, and with invariable succeſs.

The blackening of the skin by the internal exhibition of Nitrate of Silver has also been mentioned as a proof of medicinal absorption. But this must not be received too hastily. Analogy renders it highly probable that medicines are decomposed by the proceſs of digestion into their pristine elements. In this state they may be absorbed into the circulation. "But when thrown into the secretions or excretions, being removed beyond the controul of the vital energies, chemical affinities are sometimes again brought into play, by which these substances are in part or wholly regenerated." Such may be the case with Nitrate of Silver. At any rate whether this explanation be received or not, certain it is that many substances are displayed in some of the

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secretions which never existed in the blood. No one pretends ever to have discovered Uric acid in the blood; yet this substance is found in the Urine. In Jaundice, the skin is tinged of a deep saffron colour; owing as it has been supposed to the absorption of Bile. But neither has the colour or taste of bile ever been perceived in the Serum of the blood, or Urine. Numerous other circumstances to the same purport might be mentioned: but these examples will suffice to show that because a substance is found in a particular situation, it is no proof that it must have paſsed there through the circulation in its original state. It was stated by one of the older physiologists, Boerhave, I believe, that Mercurial globules were actually seen in the bones. Now can we for a moment suppose that a substance whose specific gravity is at least twelve times

greater than that of the blood, could circulate with this fluid through all parts of the body? The idea is at once ridiculous and absurd. Besides, extraneous bodies are often found in different parts of the body. Last winter in dissecting a gentleman, a needle was discovered occupying one of the Lungs. Are we to be told by the advocates of Medicinal absorption that this needle could only have reached the pulmonary organs through the medium of the circulation?— I mention this circumstance, not because I suppose there any so stupid as to believe the latter explanation, but merely to show to what ridiculous consequences the doctrine if extended would lead.

Another circumstance which has been supposed to favour the doctrine of Medicinal Absorption is that the

colouring matter of Rhubarb has been perceived in the Urine after the exhibition of this article. Now here I may very properly recur to the old interrogatory — if the Rhubarb paſsed the rout of the circulation, why is not its colour visible in the blood? This objection is supposed to be done away by answering that the Rhubarb is diffused through such a large maſs of fluid, it is impoſsible that its properties should be perceptible: but that when condensed into a smaller compaſs in an excretion, as the urine; then its colour is rendered sensible. This explanation is not only a sly subterfuge, but it is an absolute untruth. To satisfy myself on this point, I made two or three experiments. In the first I took thirty-two pints of limpid colourleſs water: into this I slowly introduced half a drachm of Rhubarb. Upon stirring

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the mixture, I perceived the whole had a yellow tinge. Again, I dropped a single grain of Rhubarb into a quart of water, and found that even this large quantity was sensibly coloured. Now twenty-four pints is the medium quantity of blood generally met with in the human system: half a drachm therefore of Rhubarb, which is the usual dose, it is obvious ought to colour the whole mass of circulating fluids. And when we recollect that the Serum, in which alone the colour could be perceived, does not constitute one half part of the blood, we must be struck with the fact that this fluid ought to have a deep tinge; the quantity being only twelve pints.

But if Rhubarb passed the rout of the circulation to get to the bladder, why I may ask is it not perceptible in some

of the other secretions, as well as the urine? Here we are very seriously told that the urine is an excretion, destined to carry off all recrementitious matters, and that Rhubarb is among the substances of this description. And what I may enquire is the matter of perspiration? Certainly this is also an excretion; and being in a much smaller quantity than the urine, it should be much more deeply coloured. It follows therefore that Rhubarb never could have entered the blood.

But I will go a step farther. I am now to combat the doctrine on the broad ground that there is a direct communication between the Alimentary Canal and Bladder. This opinion would not appear improbable from the numerous inosculations among the lymphatics of those parts. The supposition is also strengthened by the fact of the very speedy passage of

certain acidulous waters. But what puts the matter beyond all poſsible doubt, is that although a ligature be paſsed around both the Ureters, yet in due time the bladder will be filled with urine. The fact therefore of Rhubarb being found in the urine, so far from proving medicinal absorption, rather tends to a contrary belief, in as much as it demonstrates that substances can be found in apparently unnatural positions without ever entering the blood.

It has been said that after the liberal internal exhibition of Tincture of Cantharides, the skin has been observed to become vesicated. Admitting the truth of the fact, and I am by no means disposed to doubt it, it does not at all prove that the medicine paſsed into the blood-veſsels in order to arrive at the skin. For how can we believe that a

substance so acrid and irritating as Cantharides could mix itself with a vital fluid like the blood, and move in immediate contact with the delicate internal coats of the arteries and veins with impunity, and yet vesicate the comparatively dense and tough texture of the skin? The idea is strange, and appears altogether inconsistent and unnatural. I am not here bound as before to demonstrate a direct paſsage from the stomach to the skin. It is enough that the substance never entered the bloodveſsels, and this I think I have sufficiently shown.

There are many other arguments used for the same purpose. But the answers to them are alike simple: so that it will not be neceſsary to enter into any more minuteneſs of detail. The supposed proofs of medicinal absorption are weak and illusory: and

as well might its advocates attempt to

——"Swim with fins of lead,
Or hew down oaks with rushes,"

as undertake the sustentation of their doctrine on such slender grounds as those they have advanced.

It follows therefore from the above remarks that we are to reject altogether the medication of the blood as the means by which remediate impreſsions are made on the human system.

What then remains? Are we to fold our arms in quietneſs and ease, content with the present attainments of science, or rush headlong (and blind-folded into practice? Thanks to the brightneſs of genius, neither of these unhappy alternatives now remains. In a beautiful modern theory we have a full and satisfactory explication of all the phenomena

concerned in the Modues Operandi of medicines. This doctrine though simple, and well-substantiated, has nevertheleſs paſsed through the fiery ordeal of rigid criticism. The ignorant have broken out against it in the most bitter invectives; while even the learned have received it with silent contempt, or cold disdain. The jealous have raised their feeble voices in its disparagement, and "Sympathy" has been the by-word and ridicule of every taunting slanderer and malicious satyrist. Notwithstanding this however truth will prevail, and up from the dilapidated walls of detraction and jealousy it shall rise victorious, arrayed in all the grandeur of magnificence, and glory of triumph.

But it is time to enter upon the subject under consideration. The doctrine to which I alluded in the former paragraph, and

for the support of which, if any it wants, I shall lend my feeble aſsistance, alleges that medicines "all act by exciting a local impreſsion, which is extended through the medium of sympathy". By Sympathy, or consent of parts is to be understood, that property of the animal economy by which an impreſsion made on one part is propagated to another. Thus head-ache is caused by Gastric derangements: itching of the nose, by worms: pain in the shoulder by Hepatic affections: pain in the knee by disease of the Hip-joint &c. The existence of these sympathetic actions is as indubitable as it is neceſsary. The only question is, in what does Sympathy consist? Notwithstanding all the researches of physiologists, little or no light has been thrown on this interesting subject. "The word Sympathy", says Bichat, "is only a veil for our ignorance in respect to the relation of the organs to each other." The existence of

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Sympathy is known only from its effects, the cause being not at all understood. "In employing the term therefore," says Dr. Chapman, "we mean only to denote a principle or power, of which we know nothing, except from the experience of its effects, the precise eſsence or nature being occult and concealed". The term we use to designate the "particular effect, is of no importance, if we but know what idea we wish to convey. "The word Sympathy", says Bichat, "is of, but little consequence, provided what it expreſses be understood."

The cause then of Sympathy being concealed, but its existence undoubted, it becomes a matter of enquiry, in what manner are these impreſsions extended? This medium of conveyance is very naturally supposed to be the nerves. When we recollect the extensive distribution and intimate connection of these organs, we must

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be sensible of the facility with which impressions could be conveyed to every part of the system. But if the nerves be the means of conveyance, how does it happen that sympathetic actions take place between parts which have no visible nervous communication whatever? Here it is to be recollected that "the nervous system brings every sentient and irritable part, under the immediate influence of the Sensorium Commune, the brain; and that therefore, all the parts of the body have a continuous nervous connection with each other, through the medium of this common centre of feeling." It is not surprizing then that impressions made on one part of the system may be extended to the brain, and from thence to another part, and that thus sympathetic actions may take place between parts that have not apparently the most distant nervous connection.

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These explanatory remarks will prepare the way for the remaining observations I have yet to make, and which will conclude this imperfect treatise.

The theory of the Modus Operandi of medicines which I wish to impress, is simply this. "Whenever a medicinal substance is applied to a susceptible portion of the body, externally or internally, an action is excited which is extended more or less, according to the diffusibility of the properties of the substance, or the degree of sympathetic connection which the part may maintain with the body generally." That this is the true mode by which medicines produce their effects, is I think pretty evident. We know very well that morbid impressions made on a part are conveyed through the medium of Sympathy: and it is therefore ver

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very reasonable to suppose that salutary impressions should be extended in the same way. But the narrow limits to which I am necessarily confined prevent my going any fuller into the arguments by which this theory of the Modus Operandi of Medicines is supported. Suffice it to say that the doctrine accounts beautifully for many operations that take place in the human system. Thus when ardent spirit is exhibited in any quantity, the brain is almost instantaneously affected; and this effect cannot possibly be accounted for on any other principle than the sympathetic extension of the original local impression.

The reason why a medicine operates upon one particular part in preference to another cannot at all be explained.

neither indeed is it neceſsary. Certain it is that every organ has its peculiar and appropriate stimulus: as light to the eye: sound to the ear, &c. The circumstance therefore need not astonish us; and the doctrine of Sympathy is not at all defective on this account.

On the whole, this mode of explaining the operation of Medicines appears the most intelligible, rational and compatible with the present state of science. And accordingly the opinion is embraced by some of the most ingenious and scientific of Physiologists and Philosophers.

I have thus in as concise a manner as poſsible given a condensed account of the principal circumstances connected with the Modus Operandi of Medicines

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The subject it is true is intricate and altogether speculative; and I incur and may perhaps merit severe censure for engaging in it.

I cannot however conclude without making one more remark. — I am well aware that it has been considered by some a matter of no importance whether we understand the manner in which medicines operate or not. Such a doctrine however is the very bane of science. It gives open countenance to scepticism, and prostrates every ennobling sentiment of investigation and research. It encourages ignorance, hoists the flood-gates of error, and lights the torch of chicanery and empiricism. True it is that when we soar too high on the aerial pinions of theory and speculation, we are lia

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liable to be led into error. But restrained within its proper boundaries, I do maintain that theorizing is perfectly safe: and it is the only poſsible means of explaining many of the secret operations of nature, shrouded as they are by the opaque caparison of obscurity. Let the consideration then of former achievements stimulate to a more ardent enthusiasm, by which truth may be confirmed and science benefited.

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Deposited March 8th 1854

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